mmol) were dissolved in 10 mL of dry DMF. The reaction mixture was heated at 90 °C for 4 days and then cooled to rt quenched with dilute HCl and extracted several times with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by flash column chromatography eluting first with 20% EtOAc–hexane to recover starting material 17 (75 mg, 20%), followed by 25% EtOAc/5% acetic acid/hexane to give the desired carboxylic acid as a white solid that was recrystallized (341 mg, 77%): mp 107–108 °C (Et_2O–hexane); $[\alpha]^{20}_D$ = −143.70° (c = 1.66, $CHCl_3$); ^1H NMR δ 7.25–7.34 (m, 5 H), 7.06 (s, 4 H), 5.27 (bd, J = 8.7 Hz, 1 H, HN), 4.65 (dd, J = 8.7, 5.5 Hz, 1 H, H-2), 4.24 (d, J = 5.5 Hz, H-3), 3.59 (d, J = 13.3 Hz, 1 H), 3.46 (d, J = 13.3 Hz, 1 H), 2.30 (s, 3 H), 1.37 (s, 9 H); ^{13}C NMR δ 174.5, 155.3, 138.1, 136.9, 133.9, 129.2, 128.9, 128.6, 127.9, 80.5, 58.1, 50.8, 35.5, 28.2, 21.1; MS m/z 401 (M + 1, 12). Anal. Calcd for $C_{22}H_{27}O_4NS$: C, 65.81; H, 6.78; N, 3.48. Found: C, 65.83; H, 6.92; N, 3.57.

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Formation and Alkylation of Anions of Bis(methylsulfonyl)methane

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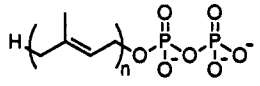
This study of the formation and alkylation of anions of a 1,3-disulfone was undertaken to explore the idea that the disulfone moiety might serve as a surrogate for the diphosphate group in prospective inhibitors of the important enzymatic reactions which have substituted diphosphates as substrates. The diphosphate moiety itself is unsuitable as part of substrate analogue inhibitors in vivo because it is readily hydrolyzed by phosphates and because, being ionic, it presumably would have difficulty crossing cell membranes.[1] Sulfones have previously been proposed as nonionic, nonhydrolyzable substitutes for biological phosphodiesters.[2] The specific context in which it was decided to explore the idea of 1,3-disulfones as diphosphate mimics was that of prenylated diphosphates 1, which are



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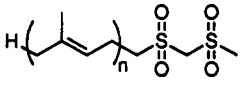

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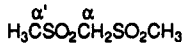

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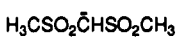

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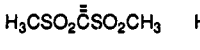

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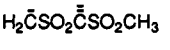

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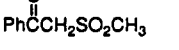

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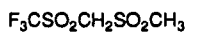

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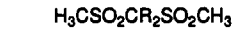
key intermediates in the biosynthesis of important natural products such as steroids 1 (n = 1–3)[3,4] and prenylated proteins 1 (n = 3,4).[4,5] The analogous prenylated 1,3-disulfones 2 are very similar in size and shape to the natural substrates, as judged from CPK models and Chem-X modeling program studies; they would clearly not be readily hydrolyzed, and they might be sufficiently polar to bind in the active site in place of the ionic diphosphate moiety.[5]

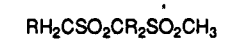
The most direct method for synthesis of the desired 1,3-disulfones 2 appeared to be alkylation with the appropriate allylic halide at the anionic site formed from a methyl group (α′ position) of bis(methylsulfonyl)methane (3).[6] As expected, initial deprotonation of 3 to form an anion occurs at the doubly activated methylene group (pK_a = 12.54)[7] to form α-monoanion 4, but it was unknown whether a second deprotonation would generate the desired nucleophilic properties at the terminal α′-position via formation of dianion 5 or would lead instead to α,α-dianion 6. If the latter were formed, a third deprotonation to form α,α,α′-trianion 7 presumably would be required in order to effect the desired α′-alkylation. Prior studies of alkylation of substrates most closely related to 3 have indicated that the α,α′-dianion is formed in the case of β-keto sulfone 8,[8] but that the α,α-dianion is formed from trifylsulfone 9,[9,10] so that it was unclear what sequence of deprotonation to expect from 3. Accordingly, determination of this sequence was undertaken with 3, which we found can be most conveniently prepared from commercially available methyl methylsulfinylmethyl sulfide by Oxone oxidation.[11]

The first method employed consisted in treatment of THF solutions of 3 with 1, 2, or 3 equiv of n-BuLi at rt for 30 min, followed by rapid addition of a large excess of MeI. After 1 h at rt, these reactions afforded essentially quantitative yields of the α-monomethylated, α,α-dimethylated, and α,α,α′-trimethylated bis(methylsulfonyl)methanes 10, 11, and 12, respectively. If the

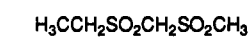
10, R = CH_3
13, R = D



11, R = CH_3
14, R = D



12, R = CH_3
15, R = D



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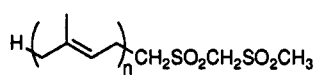
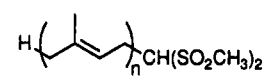


17, n = 1
19, n = 2
21, n = 3



18, n = 1
20, n = 2
22, n = 3

reaction time was abbreviated by immediate evaporation of the reaction mixture after addition of excess MeI to the

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anionic solutions, 77% of **10**, 77% of **11**, and 85% of **12** were isolated. These results are consistent with an order of anion formation from **3** of **4**, then **6**, and then **7**, and are analogous to those obtained by Hendrickson[9,10] upon alkylation of di- and trianions of **9**, except that the more stable monoanion of **9** survived unalkylated under the conditions used. In the case of **3**, the initial treatment of its THF solution with base in all cases produced a cloudy mixture which became more opaque as the number of equivalents of *n*-BuLi was increased. These observations contrast with those cited for **9**: an α-monoanion soluble in THF, an insoluble α,α-dianion, but, curiously, an α,α,α'-trianion which is again soluble.[10]

Although the methylation results strongly suggested that the deprotonation sequence of **3** is α, α, and then α', concern about the heterogeneity of the reaction mixtures and the noninstantaneous nature of the methylation reactions led us to attempt a more rigorous determination of the composition of anionic species formed from **3**. Accordingly, treatment of **3** with 1, 2, or 3 equiv of *n*-BuLi at rt for 2 h was followed by rapid addition of the same number of equivalents of CH_3COOD and immediate solvent evaporation to afford a crude product which was analyzed by NMR without purification. The limited amount of CH_3COOD and the minimized, rapid workup conditions were adopted because it was observed that use of either excess CH_3COOD or aqueous workup conditions led to isotopic exchange at the α position of **3**.[7] The ^1H and ^2H NMR spectra of the crude products thus obtained were compared with the ^1H NMR spectrum of **3**, which shows peaks at δ 3.25 (t, $J_{\alpha'H\alpha H}$ = 0.9 Hz, 6 H) for the α' protons and 5.06 (septet, $J_{\alpha H\alpha'H}$ = 0.9 Hz, 2 H) for the α protons.

When 1 equiv of *n*-BuLi and CH_3COOD were used, the product showed only broadened singlets at δ 3.26 (6 H) and 5.06 (1 H) in its ^1H NMR spectrum and at δ 4.93 in its proton-decoupled or -coupled ^2H NMR spectra, consistent with the expected monodeuterated product **13**, in which neither the small $\alpha'H\alpha H$ coupling seen in **3** nor the $\alpha H\alpha D$ coupling was resolved. When 2 equiv of *n*-BuLi and CH_3COOD were used, the crude product showed essentially only a singlet at δ 3.26 in its ^1H NMR spectrum and a singlet at δ 4.93 in its ^2H NMR spectrum (Figure 1a), consistent with structure **14**, confirming that the sequence of deprotonation of **3** was α,α to form dianion **6** rather than α,α' to form dianion **5**. Treatment of **3** with 3 equiv of base and electrophile then provided the results expected for formation of α,α,α'-trianion **7**. The ^1H NMR spectrum of the crude product displayed a singlet at δ 3.26 and a 1:1:1 triplet at 3.24 ($J_{\alpha'H\alpha D}$ = 2.0 Hz), the proton-decoupled ^2H NMR spectrum contained singlets at δ 4.93 and 3.21, and the proton-coupled ^2H NMR spectrum (Figure 1b) showed a singlet at δ 4.93 and a 1:3:1 triplet at 3.21 ($J_{\alpha'D\alpha'H}$ = 2.0 Hz), entirely consistent with the α,α,α'-trideuterated **15**. The slight upfield shift of 0.02 ppm in the ^1H NMR spectrum of **15** for the α' protons upon monodeuteration is a typical shielding effect of such isotopic substitution.[12]

The results described above engendered optimism that prenylation of **3** to **2** might be efficiently accomplished by treatment of putative trianion **7** with 1 equiv of the appropriate allylic halide to effect selective substitution at the most basic α' position. This desired selectivity was explored first by use of 1 equiv of MeI as electrophile. Unfortunately, treatment of **7** with 3 equiv of base, usually *n*-BuLi, followed by addition of 1 equiv of MeI, under a variety of experimental conditions, led to complex mixtures

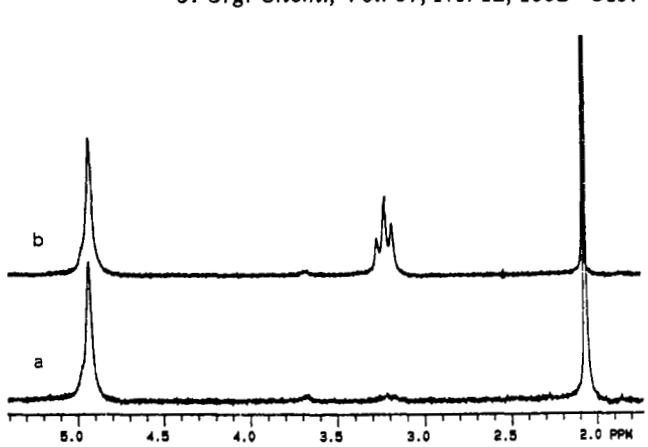

Figure 1. Proton-coupled ^2H NMR spectra in H_3CCOCH_3, referenced to D_3CCOCD_3 as δ = 2.07 ppm, of (a) α,α-dideuteriobis(methylsulfonyl)methane (**14**) and (b) α,α,α'-trideuteriobis(methylsulfonyl)methane (**15**).

which ^1H NMR analysis indicated to contain usually about 40% of a roughly 3:2 ratio of **16**, δ 1.38 (t, J = 7.0 Hz, 3 H) and 3.45 (q, J = 7.0 Hz, 2 H), and the familiar **10**, δ 3.24 (s, 6 H) and 4.96 (q, 1 H). Despite extensive efforts, including normal- and reverse-phase TLC, HPLC, and gradient flash chromatography, it proved impossible to separate the mixture of these two monomethylation products. Similar frustration was encountered in Hendrickson's laboratory when selective α'-alkylation of the trianion of trifylsulfone **9** was attempted.[10] Treatment of the trianion from **9** with 1 equiv of MeI or benzyl bromide under a variety of conditions invariably led to a mixture of α'- and α-alkylation products, a result suggested[10] to be the result of decreased stabilization, and therefore increased reactivity, of the α dianionic center by the sulfonyl group adjacent to the α' anion upon its formation.

Although the results of the attempted selective α'-methylation of **3** were disappointing, it was still hoped that this approach might suffice for synthesis of **2**, so attention was turned to the latter. When **7** was treated sequentially with 3 equiv of *n*-BuLi and 1 equiv of prenyl bromide, alkylation proved to be more regioselective, affording reliably an approximately 9:1 ratio of **17** to **18**. Perhaps the greater regioselectivity simply reflects the greater steric demand of the primary, as opposed to methyl, halide as electrophile. However, the crude combined yield of **17** plus **18** was still only about 35%, with considerable amounts of both unchanged **3** and byproducts which resisted identification also being formed. Essentially the same results were obtained when either geranyl bromide or farnesyl bromide was used as electrophile in efforts to prepare **19** or **21**.

Numerous experimental variables were modified in efforts to improve the yield of α'-prenylation, in major part guided by the suspicion that the inefficiency of alkylation was related to the heterogeneous nature of the reaction mixture.[13] However, none of these was successful in generating a homogeneous trianion solution or in markedly increasing the yield of alkylation. The least inefficient method for the preparation of the desired α'-alkylated **17**, **19**, and **21** eventually proved to be treatment of the cloudy mixture of **7** in THF with 0.33 equiv of alkyl halide. This afforded the cleanest product and in the highest yield (25–35%, based on allyl halide). Identification of **17**, **19**, and **21** was readily made on the basis of their ^1H NMR spectra, which showed a 2 H singlet at 5.0 ppm for the α

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methylene protons and a 3 H singlet at 3.26 for the remaining α' methyl protons.

Preparation of pure samples of the alternative α-alkylation products **18**, **20**, and **22** was accomplished by use of 2 equiv of *n*-BuLi in THF to form α,α-dianion **6**, followed by 0.5–0.33 equiv of prenyl halide as the limiting reagent, to lead, respectively, to 51% of **18**, 53% of **20**, and 49% of **22**. The identity of these α-prenylated compounds was evident from the appearance in their ^{1}H NMR spectra of a 6 H singlet at δ 3.32 for the two α'-methyl groups and a 1 H triplet at 4.72 for the α-methine proton. Attempts to improve the efficiency of α-alkylation also failed. Reactions of monoanion **4** gave lower yields of pure products.

These studies have clearly established the sequence of anion formation from 1,3-disulfone **3**. They have also been successful in leading to the direct, one-step preparation of the desired prospective diphosphate surrogates **17**, **19**, and **21**, although the inability to effect higher yield of selective alkylation at the α'-position remains disappointing.

Experimental Section

NMR spectra were determined at the following frequencies: ^{1}H, 299.95 MHz, ^{13}C, 75.430 MHz, and ^{2}H, 46.044 MHz. ^{1}H NMR spectra are reported as δ values in D_3CCOCD_3 with respect to tetramethylsilane. ^{2}H NMR spectra are reported as δ values in H_3CCOCH_3 and are referenced to D_3CCOCD_3 as δ = 2.07 ppm. HPLC was performed on a Waters Model 510 solvent delivery system with a Model 481 Lambda-Max variable wavelength detector, a Model U6K universal injector, and a Beckman Ultrasphere C18 column (5 μm, 250 × 4.5 mm) at ambient temperature, with attenuation of 0.5 AUFS and detection wavelength of 210 nm. The HPLC solvents were prepared by filtering the appropriate solutions through a 0.2-μm nylon 66 membrane, followed by degassing with He. The mobile phase and flow rate are as indicated. Flash chromatography was carried out by the method of Still[14] on Kieselgel 60 silica (230–400 mesh). All reagents were purchased from Aldrich Chemical Co., Milwaukee, WI. THF was distilled from sodium metal with benzophenone indicator. MeI and allylic bromides were distilled prior to use. CH_3CO_2D was dried over molecular sieves (4A) for 12 h prior to use. Titration of *n*-butyllithium in hexanes (*n*-BuLi) with Ph_2CHCO_2H in THF was performed in duplicate prior to use. Potassium hydride (KH, 25.6% in oil) was washed with hexanes (3 × 20 mL) and dried by passing N_2 over the white powder. 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-crown-6) was dried under reduced pressure over P_2O_5 overnight prior to use. Brine refers to a saturated aqueous NaCl solution. Anhydrous reactions were performed in glassware that had been flame-dried or heated in an oven overnight at 125 °C and then cooled in a desiccator containing $CaSO_4$ or P_2O_5. All reactions were carried out at rt unless otherwise specified. The term "under N_2" or "under Ar" refers to the maintenance of a positive pressure of that gas which had been passed through a column of anhydrous $CaSO_4$.

Bis(methylsulfonyl)methane (3). In the manner of Trost,[11] to a solution of 1.70 mL (16.3 mmol) of methyl methylsulfinylmethyl sulfide in 65 mL of MeOH at 0 °C was added a slurry of 44.6 g (72.4 mmol) of Oxone in 97.0 mL of H_2O. The resulting mixture was stirred at 0 °C for 9 h. The aqueous layer was extracted with EtOAc (5 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated to give 2.58 g (92%) of **3** as a white solid after recrystallization from 4:1 EtOH–H_2O: mp 147.8–148.5 °C (lit.[6] mp 147–148.5 °C); ^{1}H NMR δ 5.06 (septet, J = 0.9 Hz, 2 H), 3.25 (t, J = 0.9 Hz, 6 H) (lit.[11] ^{1}H NMR(DMSO-d_6) δ 5.42 (m, J = 0.6 Hz, 2 H), 3.22 (t, J = 0.6 Hz, 6 H)); ^{13}C NMR (D_3CCOCD_3) δ 71.4, 42.1.

1,1-Bis(methylsulfonyl)ethane (10). To a solution of 0.259 g (1.50 mmol) of **3** in 250 mL of THF was added 1.00 mL (1.52 mmol) of *n*-BuLi. The solution was stirred for 30 min under N_2, and 5.00 mL (80.3 mmol) of MeI was added all at once. The solution was stirred for 1 h, and then 25.0 mL of H_2O was added. The THF was evaporated, and the remaining aqueous solution was extracted with EtOAc (3 × 25 mL). The combined orgnic extracts were evaporated to give 0.309 g (100%) of crude **10** as a very light yellow solid. Recrystallization from 4:1 EtOH–H_2O gave 0.260 g (93%) of colorless **10**: mp 122–123 °C (lit.[6] mp 122 °C); ^{1}H NMR δ 4.96 (q, J = 7.4 Hz, 1 H), 3.24 (s, 6 H), 1.77 (d, J = 7.4 Hz, 3 H).

Alternatively, evaporation of an analogous reaction mixture immediately after addition of MeI, flash chromatography of the residue (4:1 EtOAc–hexane), partitioning of eluted material between EtOAc and H_2O, and crystallization of the EtOAc extract from 1:1 EtOH:H_2O afforded 77% of **10**, mp 122–124 °C.

2,2-Bis(methylsulfonyl)propane (11). Exactly the same procedure used for **10** was employed with 0.12 g (0.70 mmol) of **3** and 0.91 mL (1.4 mmol) of *n*-BuLi to afford 0.14 g (100%) of **11** as a very light yellow solid. Recrystallization from 4:1 EtOH–H_2O gave 0.14 g (100%) of colorless **11**: mp 117–118 °C (lit.[15] mp 118 °C); ^{1}H NMR δ 3.24 (s, 6 H), 1.75 (s, 6 H).

The alternative procedure gave 77% of **11** in two crops, mp 113–117 °C.

2-(Ethylsulfonyl)-2-(methylsulfonyl)propane (12). Exactly the same procedure used for **10** was employed with 0.160 g (0.929 mmol) of **3** and 1.85 mL (2.81 mmol) of *n*-BuLi to afford 0.223 g (114%) of **12** as a light yellow solid. Recrystallization from isopropyl alcohol gave 0.193 g (97%) of colorless **12**: mp 77–78 °C; IR (KBr) 1320, 1120 cm^{-1}; ^{1}H NMR δ 3.49 (q, J = 7.5 Hz, 2 H), 3.25 (s, 3 H), 1.76 (s, 6 H), 1.37 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 81.7, 44.7, 38.3, 16.9, 5.2. Anal. Calcd for $C_6H_{14}S_2O_4$: C, 33.62; H, 6.59. Found: C, 33.48; H, 6.63.

This alternative procedure gave 85% of **12**, mp 76–77.5 °C.

Bis(methylsulfonyl)monodeuteriomethane (13). To a solution of 1.0 g (5.8 mmol) of **3** in 100 mL of THF was added 3.7 mL (5.9 mmol) of *n*-BuLi. The solution was stirred for 2 h under N_2, and 0.34 mL (5.9 mmol) of CH_3CO_2D was added. The solvent was evaporated, and the crude **13** was dried at 0.2 Torr over P_2O_5: ^{1}H NMR δ 5.06 (bs, 1 H), 3.26 (s, 6 H); ^{2}H NMR (^{1}H decoupled) δ 4.93 (s); ^{2}H NMR (^{1}H coupled) δ 4.93 (s).

Bis(methylsulfonyl)dideuteriomethane (14). Exactly the same procedure was employed with 7.5 mL (12 mmol) of *n*-BuLi and 0.68 mL (12 mmol) of CH_3CO_2D to afford **14**: ^{1}H NMR δ 3.26 (s); ^{2}H NMR (^{1}H decoupled) δ 4.93 (s); ^{2}H NMR (^{1}H coupled) δ 4.93 (s).

(Monodeuteriomethylsulfonyl)(methylsulfonyl)dideuteriomethane (15). Exactly the same procedure was employed with 11.0 mL (17.6 mmol) of *n*-BuLi and 1.02 mL (17.7 mmol) of CH_3CO_2D to afford **15**: ^{1}H NMR δ 3.26 (s, 3 H), 3.24 (1:1:1 t, J = 2.0 Hz, 2 H); ^{2}H NMR (^{1}H decoupled) δ 4.93 (s), 3.21 (s); ^{2}H NMR (^{1}H coupled) δ 4.93 (s), 3.21 (1:3:1 t, J = 2.0 Hz).

(*E*)-3,7-Dimethyl-2,6-octadienyl Bromide (Geranyl Bromide). According to an unpublished procedure of Edstrom,[16] to a solution of 2.0 mL (12 mmol) of *trans*-geraniol in 10 mL of hexane at 0 °C in a flask wrapped in Al foil was added 0.36 mL (3.8 mmol) of PBr_3. The mixture was allowed to warm to 24 °C and stirred under N_2 for 18 h, and 5.0 mL of 5% aqueous $NaHCO_3$ solution was added. The aqueous layer was removed after gas evolution ceased. Evaporation of solvent and vacuum distillation gave 2.0 g (82%) of *trans*-geranyl bromide: bp 72 °C (0.6 Torr) (lit.[17] bp 110 °C (3 Torr)); ^{1}H NMR δ 5.35 (t, J = 7.2 Hz, 1 H), 5.08 (br s, 1 H), 4.05 (d, J = 8.4 Hz, 2 H), 2.20–1.95 (m, 4 H), 1.72 (s, 3 H), 1.66 (s, 3 H), 1.59 (s, 3 H) (lit.[17] ^{1}H NMR (CCl_4) δ 5.46 (br t, J = 8 Hz, 1 H), 5.02 (br s, 1 H), 3.95 (d, J = 8.0 Hz, 2 H), 2.05 (m, 4 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.58 (s, 3 H)).

(*E*,*E*)-2,6,10-Trimethyl-2,6,10-tridecatrienyl Bromide (Farnesyl Bromide). Exactly the same procedure was applied to 1.0 mL (4.0 mmol) of *trans,trans*-farnesol to afford 0.92 g (82%) of *trans,trans*-farnesyl bromide: bp 80 °C (0.05 Torr) (lit.[18] bp 100–110 °C (0.15 Torr)); ^{1}H NMR δ 5.51 (t, J = 8.0 Hz, 1 H), 5.09 (m, 2 H), 3.99 (d, J = 9.0 Hz, 2 H), 2.20–1.90 (m, 8 H), 1.71 (s, 3 H), 1.65 (s, 3 H), 1.59 (s, 3 H), 1.58 (s, 3 H), (lit.[18] ^{1}H NMR δ 5.52 (t, J = 9 Hz, 1 H), ~5.09 (br s, 2 H), 3.95 (d, J = 9 Hz, 2

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H), 2.2–2.0 (m, 8 H), 1.69 (s), 1.61 (s) (12 H)).

((4-Methyl-3-pentenyl)sulfonyl)(methylsulfonyl)methane (17). To a solution of 0.53 g (3.0 mmol) of **3** in 125 mL of THF was added 6.1 mL (9.4 mmol) of *n*-BuLi. The solution was stirred under Ar for 1 h, and then 0.12 mL (1.0 mmol) of prenyl bromide was added all at once. The mixture was stirred for 23 h, and then 1.5 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the 2.9 g of wet residue was purified by flash chromatography (1:1 EtOAc–hexane) to afford 0.11 (g (44% based on prenyl bromide) of a 6:1 mixture of **17** and **18**. Gradient flash chromatography (1:9–2:3 EtOAc–hexane) gave 0.087 g (35%) of **17** which, after crystallization from MeOH, had mp 62–63 °C: IR (KBr) 1310, 1125 cm^{-1}; ^1H NMR δ 5.20 (t, J = 7.3 Hz, 1 H), 5.01 (s, 2 H), 3.42 (m, 2 H), 3.26 (s, 3 H), 2.55 (m, 2 H), 1.69 (s, 3 H), 1.65 (s, 3 H); the multiplets at 3.42 (AA′) and 2.55 (BB′) could be simulated by use of the LAOCOON III program[19] with $J_{AA'} = J_{BB'} = 14.0$ Hz, $J_{AB'} = J_{A'B} = 7.1$ Hz, $J_{AB} = J_{A'B'} = 12.5$ Hz, and $J_{BvinylH} = J_{B'vinylH} = 7.3$ Hz; ^{13}C NMR (D_3CCOCD_3) δ 135.6, 120.6, 70.1, 54.0, 42.4, 25.7, 21.0, 17.7. Anal. Calcd for $C_8H_{16}S_2O_4$: C, 39.98; H, 6.71; S, 26.68. Found: C, 39.68; H, 6.65; S, 26.85.

1,1-Bis(methylsulfonyl)-4-methyl-3-pentene (18). To a solution of 4.0 g (23 mmol) of **3** in 200 mL of THF was added 30 mL (45 mmol) of *n*-BuLi. The solution was stirred under N_2 for 30 min, and 1.4 mL (12 mmol) of prenyl bromide was added all at once. The mixture was stirred for 15 h, and then 20 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (5.5 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 1.5 g (51% based on prenyl bromide) of **18** as a clear oil. Crystallization from 4:1 EtOH–H_2O afforded 1.4 g (48%) of **18**: mp 70.1–72.0 °C; IR (KBr) 1310, 1135 cm^{-1}; ^1H NMR δ 5.37 (t, J = 7.2 Hz, 1 H), 4.72 (t, J = 6.0 Hz, 1 H), 3.23 (s, 6 H), 2.98 (t, J = 6.6 Hz, 2 H), 1.72 (s, 3 H), 1.70 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 136.1, 119.7, 81.2, 41.3, 25.8, 23.8, 17.8. Anal. Calcd for $C_8H_{16}S_2O_4$: C, 39.98; H, 6.71. Found: C, 40.09; H, 6.72.

Alternatively, use of the detailed procedure described below for preparation of **20** on 0.53 g (3.1 mmol) of **3** under Ar afforded 47% of **18**. If the addition of *n*-BuLi were omitted from that procedure, 47% of **18** was obtained from 0.48 g (2.8 mmol) of **3**.

((4,8-Dimethyl-3,7-nonadienyl)sulfonyl)(methylsulfonyl)methane (19). To a solution of 0.50 g (2.9 mmol) of **3** in 250 mL of THF was added 7.8 mL (8.7 mmol) of *n*-BuLi. The solution was stirred under N_2 for 1 h, and 0.20 mL (1.0 mmol) of *trans*-geranyl bromide was added all at once. The mixture was stirred for 25 h, and then 25 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (0.52 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.094 g (30% based on *trans*-geranyl bromide) of a 9:1 mixture of **19** and **20**. Gradient flash chromatography (1:9–2:3 EtOAc–hexane) gave 0.078 g (25%) of **19** as a light yellow oil: IR (neat) 1335–1305, 1120 cm^{-1}; ^1H NMR δ 5.23 (t, J = 7.1 Hz, 1 H), 5.11 (t, J = 7.1 Hz, 1 H), 5.02 (s, 2 H), 3.44 (m, 2 H), 3.26 (s, 3 H), 2.57 (m, 2 H), 2.15–1.95 (m, 4 H), 1.68 (s, 3 H), 1.66 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 139.2, 131.9, 124.7, 120.5, 70.1, 53.9, 42.3, 40.2, 27.1, 25.8, 20.9, 17.7, 16.1. Anal. Calcd for $C_{13}H_{24}S_2O_4$: C, 50.62; H, 7.84. Found: C, 50.60; H, 7.85.

1,1-Bis(methylsulfonyl)-4,8-dimethyl-3,7-nonadiene (20). To a mixture of 0.28 g (7.0 mmol) of KH and 200 mL of THF was added a solution of 2.4 g (9.1 mmol) of 18-crown-6 and 0.56 g (3.3 mmol) of **3** in 60 mL of THF. The mixture was stirred under N_2 for 2.5 h at 23 °C, and 2.5 mL (3.5 mmol) of *n*-BuLi was added. The mixture was stirred for 2 h, and 0.35 mL (1.8 mmol) of *trans*-geranyl bromide was added all at once. The mixture was stirred for 24 h, and then 25 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (1.2 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.31 g (56% based on geranyl bromide) of **20** as a light yellow oil. HPLC with H_3CCN–MeOH–H_2O (45:45:10) at a flow rate of 0.5 mL/min gave an analytical sample of **20** (retention time 8.7 min): IR (neat) 1310, 1125 cm^{-1}; ^1H NMR δ 5.40 (t, J = 7.2 Hz, 1 H), 5.11 (t, J = 7.2 Hz, 1 H), 4.72 (t, J = 6.0 Hz, 1 H), 3.23 (s, 6 H), 2.98 (t, J = 6.6 Hz, 2 H), 2.15–1.98 (m, 4 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 139.8, 131.9, 124.8, 119.6, 81.3, 41.4, 40.2, 26.9, 25.8, 23.7, 17.7, 16.2. Anal. Calcd for $C_{13}H_{24}S_2O_4$: C, 50.62; H, 7.84. Found: C, 50.69; H, 7.89.

Alternatively, use of the detailed procedure described above for preparation of **18** on 0.180 g (1.00 mmol) of **3** under Ar afforded 53% of **20**.

((4,8,12-Trimethyl-3,7,11-tridecatrienyl)sulfonyl)(methylsulfonyl)methane (21). To a solution of 0.50 g (2.9 mmol) of **3** in 250 mL of THF was added 5.4 mL (8.9 mmol) of *n*-BuLi. The solution was stirred under N_2 for 5 h, and 0.21 g (0.74 mmol) of *trans,trans*-farnesyl bromide was added all at once. The mixture was stirred for 25 h, and then 25 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (0.58 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.090 g (32% based on *trans,trans*-farnesyl bromide) of a 9:1 mixture of **21** and **22**. Gradient flash chromatography (1:9–2:3 EtOAc–hexane) gave 0.063 g (23%) of **21** as a clear oil. HPLC with H_3CCN–MeOH–H_2O (37:37:26) at a flow rate of 2.0 mL/min gave an analytical sample of **21** (retention time 18.0 min): IR (neat) 1310, 1130 cm^{-1}; ^1H NMR δ 5.24 (t, J = 6.6 Hz, 1 H), 5.14 (t, J = 6.6 Hz, 1 H), 5.11 (t, J = 7.5 Hz, 1 H), 5.02 (s, 2 H), 3.44 (m, 2 H), 3.26 (s, 3 H), 2.58 (m, 2 H), 2.20–1.95 (m, 6 H), 1.69 (s, 3 H), 1.66 (s, 3 H), 1.61 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCOCD_3) δ 139.3, 135.7, 131.6, 125.1, 124.7, 120.6, 70.2, 54.0, 42.3, 40.2, 40.2, 27.4, 27.1, 25.8, 21.0, 17.7, 16.2, 16.1. Anal. Calcd for $C_{18}H_{32}S_2O_4$: C, 57.57; H, 8.59. Found: C, 57.70; H, 8.64.

1,1-Bis(methylsulfonyl)-4,8,12-trimethyl-3,7,11-tridecatriene (22). To a solution of 0.50 g (2.9 mmol) of **3** in 600 mL of THF was added 2.9 mL (4.4 mmol) of *n*-BuLi at 0 °C. The solution was stirred under N_2 for 2.5 h at 21 °C, and 0.28 g (1.0 mmol) of *trans,trans*-farnesyl bromide was added all at once. The mixture was stirred for 22 h, and then 0.5 mL of aqueous saturated NH_4Cl solution was added. The organic layer was evaporated, and the residue (1.1 g) was purified by flash chromatography (2:3 EtOAc–hexane) to afford 0.18 g (49% based on farnesyl bromide) of **22** as a yellow oil: IR (neat) 1335–1305, 1145–1125 cm^{-1}; ^1H NMR δ 5.41 (t, J = 7.2 Hz, 1 H), 5.06–5.20 (m, 2 H), 4.72 (t, J = 6.0 Hz, 1 H), 3.23 (s, 6 H), 2.98 (t, J = 6.6 Hz, 2 H), 2.15–1.95 (m, 6 H), 1.70 (s, 3 H), 1.66 (s, 3 H), 1.61 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (D_3CCN) δ 140.6, 136.1, 132.1, 125,2, 124.8, 119.2, 81.4, 42.0, 40.4, 40.2, 27.4, 27.0, 25.9, 23.9, 17.8, 16.4, 16.1. Anal. Calcd for $C_{18}H_{32}S_2O_4$: C, 57.57; H, 8.59. Found: C, 57.33; H, 8.57.

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Preparation and Ring-Opening of Benzylic and Allylic Cyclopropyl Dianions

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There are several examples of substituted cyclopropyl anions rearranging to substituted allyl anions.[1] Although the ring-opening of cyclopropyl anion to allyl anion is not known for the parent compound, it has been studied by semiempirical and ab initio methods.[2] The reaction ap-

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